

in seven U.S. cities: Chicago, Detroit, Houston, Los Angeles, Milwaukee, New York, and Philadelphia. Looking at data for 1986–1989, the researchers found that 3,250 (about 5.7%) of the cities' annual congestive heart failure hospitalizations correlated with an increase in air CO.

Thomas E. Dahms, a cardiovascular physiologist at St. Louis University who has studied CO, cautions that the study's retrospective approach is limited. "For one thing, congestive heart failure is a loosely defined diagnosis," Dahms says. "To validate its consistency between hospitals, you'd have to do some spot checking of patient records."

Dahms also worries whether air pollution readings accurately reflect an individual's exposure to CO. "There have been a number of studies trying to relate personal CO exposure levels to air readings picked up at monitoring stations 50 to 100 feet off the ground," he says. "So far, there has been little validation in relating the two."

But Joel Schwartz, an epidemiologist at the Harvard School of Public Health who wrote an editorial accompanying the study, says the work is informative. "There is certainly a chance for misdiagnosis when looking across cities," Schwartz says. "But within any one city's analysis, it shouldn't be a problem." Such misdiagnosis is absorbed during statistical analysis, he says. Schwartz adds that, despite inconsistencies, there is a clear link between personal exposure and air pollution readings: "The real question is, If I took everyone in this city, averaged their personal exposure to CO and correlated that, day to day, with the average outdoor air pollution readings, what would I find? Would the averages go up and down together? We won't know until we do more studies."

Morris agrees his findings are preliminary. "Clearly, this study raises as many questions as it answers," he says. One question involves the amount of CO that exacerbates heart problems. The health effects cited in this study occurred below federally permissible CO levels. "From the lowest levels of carbon monoxide, we are seeing an increase in hospital admissions with rising pollutant," Morris says. "If future studies do establish a minimum CO effect threshold, that may impact EPA air standards."

The EPA attempts to control CO pollution by regulating motor vehicle emissions. The Clean Air Act of 1990 strengthened tests for auto emission standards and required oxygenated gasolines, with additives to improve fuel efficiency, for metropolitan areas with high CO levels.

Morris next plans to study exposure to

another common auto pollutant: fine combustion particles. "It's possible that this pollutant, along with carbon monoxide, contributes to the heart failure admissions we reported," Morris says. "Now we've got to separate the two pollutants and find out how important each one is."

Barking up the Right Tree?

People may now have one more reason to save trees: they might someday save your life. In a recent study at the University of Illinois at Chicago, a compound called betulinic acid, derived from the bark of white birch trees, has been shown to halt the growth of melanoma cancer cells. More importantly, the compound selectively targets these cells, providing hope that a chemotherapeutic drug developed from betulinic acid will have very few side effects.

The compound was originally extracted from the bark of an African tree, *Ziziphus mauritiana lam* (Rhamnaceae). It was later found in the bark of the common white birch. Unlike extracting taxol, another chemotherapeutic substance obtained from tree bark, the process to extract betulinic acid is relatively simple, involving a chloroform extraction and crystallization process.

Betulinic acid was shown to be a highly effective antitumor agent in a study published in the October 1995 issue of *Nature Medicine*. The study reported on a successful series of cell culture experiments with four human melanoma cell lines (derived from lymph node, lung fluid, liver, and skin). The growth of the cell cultures was specifically inhibited using half the maximal effective doses of 1–5 micrograms per milliliter. Researchers tested the compound in immune-suppressed mice that had been induced to develop human melanomas. In these experiments, tumor growth was either inhibited significantly or halted in the treated group. A drug called DTIC (dacarbazine), commonly used to treat human melanoma, was used as one of the positive controls. The betulinic acid-treated mice showed three times greater tumor inhibition than the DTIC-treated mice.

"These results are very encouraging," says John Pezzuto, director of the Program of Collaborative Research at the University of Illinois. "Of the thousands of agents screened, betulinic acid is one of the best compounds to come out of our lab in the last five years." A potentially beneficial property of betulinic acid is that it does not appear to affect other human cancer cell types, suggesting a unique specificity for melanoma that may shed light on the mechanisms of this disease. Current anti-

neoplastic agents such as captothecin, taxol, and vinblastine are toxic to multiple cell types, resulting in damage to normal tissue.

Several pharmaceutical companies have shown interest in funding the development of betulinic acid. According to Pezzuto, *in vivo* tests are continuing and will be followed by rigorous toxicity testing. If the results are positive, an investigative new drug application may be filed with the FDA as early as 1996, allowing human clinical trials to begin.

In addition to treating malignant melanoma, a disease that strikes 1 in 90 Americans, the compound may someday be used to prevent and treat other skin cancers. Skin cancers, with about 800,000 new cases per year, are the most frequent type of cancer in the United States. The compound's efficacy will eventually also be tested against a variety of other tumor types such as neuroblastoma, a type of brain tumor. In addition, because of its emerging excellent safety profile, Pezzuto envisions betulinic acid's potential usefulness in consumer products such as sunscreens.

According to one expert, it may be too soon to tell the real potential for this bark extract. Antonio Buzaid, a melanoma specialist at the University of Texas MD Anderson Cancer Center, recently commented in *Science News* that "in most cases, such effective drugs don't pan out in people." This caution is echoed by Don Morton, medical director and chief of surgery at the John Wayne Cancer Institute, who conducts research on



Made in the shade. A substance isolated from the bark of white birch trees shows promise for treating melanomas.

melanoma vaccines. Morton, however, expresses optimism about the October study results and describes betulinic acid as one of the most exciting and unique compounds currently under investigation for treatment of melanoma.

An Environmental Nobel

Twenty years ago, when Mario Molina described his research to friends, they would look baffled, perhaps even a little worried about his state of mind. Then a postdoctoral fellow at the University of California, Irvine, Molina would explain how an invisible gas sprayed out of aerosol cans could float up to the stratosphere, about 8–12 miles above the earth's surface, and create havoc with the ozone, which protects living things on earth from shorter-wave length ultraviolet radiation. "Only a few people were aware of the ozone problem in those days, because it was such a specialized topic," says Molina, now a professor of environmental science at the Massachusetts Institute of Technology. "But a decade later, when the public had a better understanding of what humans can do to the planet, I became amazed at how many people were knowledgeable about the depletion of the ozone layer."

In 1995, Molina shared the Nobel Prize in Chemistry with colleagues F. Sherwood Rowland, professor of chemistry at the University of California, Irvine, and Paul Crutzen of Max-Planck Institute for Chemistry, in Mainz, Germany, for their work in atmospheric chemistry, especially on the formation and destruction of ozone. The researchers have made crucial discoveries showing how chemical emissions from air conditioners, aerosol cans, and fire

extinguishers can dramatically increase the destructive processes of the sensitive ozone layer, our planet's "Achilles heel," said the Royal Swedish Academy in its award citation on October 11. As ozone is depleted, more of the sun's dangerous ultraviolet rays can reach the earth causing additional skin cancers, cataracts, and damage to the immune system, but also harming ecosystems. By sounding the alarm about ozone damage, the researchers "have contributed to our salvation from a global environmental problem that could have catastrophic consequences," the academy said.

In 1970, Paul Crutzen was the first scientist to identify one of the important processes that create a natural balance in stratospheric ozone. Crutzen discovered that when nitrous oxide, which is produced by soil bacteria, floats up to the stratosphere, the chemical demolishes ozone molecules. Crutzen's research led directly to discoveries on the relationship between ozone destruction and freon compounds manufactured with chlorofluorocarbons (CFCs), says Jack Calvert, atmospheric scientist at the National Center for Atmospheric Research in Boulder, Colorado. "When nitrous oxides get to the stratosphere, they start a chemical chain reaction that destroys ozone, in the same way that freon does," Calvert says.

In fact, small amounts of other natural compounds, hydrogen and chlorine, also migrate from the earth's surface and break down ozone molecules in the stratosphere. But until industrial chemicals changed the atmosphere's chemical mix, this destruction was generally balanced by natural production of ozone. That is, the sun's rays would split oxygen molecules and start a rapid chemical reaction, leading to the for-

mation of ozone molecules. So the amount of ozone would increase or decrease by small degrees, depending on chemical influences from volcanic eruptions and seasonal changes, and on variations in the sun's intensity.

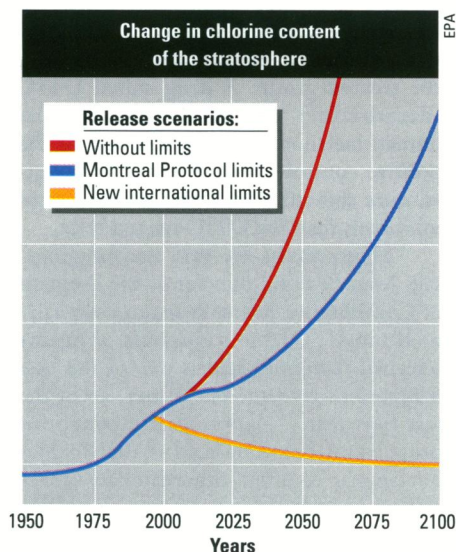
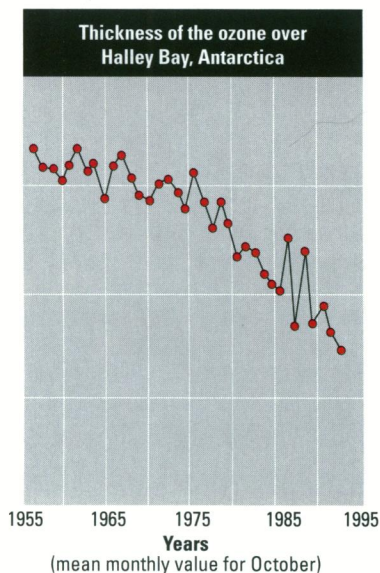
Crutzen was also among the first scientists to suspect that human-made chemicals could deplete ozone. In the early 1970s, Crutzen and Harold S. Johnston, a chemistry professor at the University of California, Berkeley, theorized that a new kind of commercial airplane called the supersonic transport (SST), which flew into the stratosphere and spewed nitrogen oxides from its exhaust, could accelerate natural destruction of ozone.

Meanwhile, by 1973, Rowland and Molina theorized that CFCs could migrate into the upper atmosphere and damage ozone. The researchers calculated that because CFCs are so stable and durable in the surface atmosphere, the chemicals can live for 50–100 years, but when they reach the stratosphere, they are disintegrated by shorter-wave ultraviolet radiation. As each chlorine molecule breaks down, it can destroy many ozone molecules, possibly depleting ozone, on a global average, by 7–13% over 100 years if CFC production continued at its rate of growth (at that time), Molina and Rowland theorized.

With further research, though, the scientists learned that ozone would be depleted in more complex ways. "Later, we realized that there would be large depletions of ozone at different latitudes, and more severe depletions at high latitudes," says Molina.

In 1975, researchers from the National Center for Atmospheric Research and the National Oceanic and Atmospheric Administration separately reported that instruments on balloons had detected abundant CFC-11 in the stratosphere. This was the first time that measurements had been made of any manufactured chlorine compounds in the upper atmosphere. The next year, a special National Academy of Sciences panel calculated that stratospheric ozone could be depleted by 7% over the long-term due to CFCs, within the range first estimated by Rowland and Molina. In presentations at scientific meetings, press conferences, and legislative hearings, Rowland and Molina began recommending a complete ban on the release of CFCs to the atmosphere.

By 1979, the United States and other nations had banned the sale of aerosol cans that contained CFCs, but companies continued to produce CFCs for other uses. Moreover, there was no urgency by the international community to ban CFCs



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